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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,883	12/21/2001	Toshio Miyata	SHIM012	2901

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EXAMINER

COUNTS, GARY W

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/936,883	Applicant(s) MIYATA, TOSHIO	
	Examiner Gary W. Counts	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 5-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 5-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The amendment filed June 7, 2004 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3, and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining the onset of renal disorders, does not reasonably provide enablement for a method for evaluating renal functions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re Wands* USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for evaluating renal functions comprising obtaining a biological specimen; contacting the sample with a reagent comprising an anti-megsin protein antibody; measuring the amount of megsin protein in the specimen; and evaluating renal functions by comparing the amount with the megsin protein amount present in a control specimen from a healthy individual.

The disclosure fails to state or teach one skill in the art how to specifically use the amount of megsin protein present in a specimen to determine renal function. The disclosure fails to show that the determination the amount of megsin protein can determine renal function. The specification on pages 15, line 37- page 16, line 21 disclose that the evaluation of renal functions means to comprehend the condition of mesangial cells, which is an important cell constructing kidney tissue, and to determine the presence or severity of a renal disease causing abnormalities in mesangial cells. The specification on page 16, lines 22-36 discloses that to evaluate renal functions according to the present invention, a biological specimen from an individual whose renal function should be tested is obtained and the concentration of megsin protein therein is measured. The amount of megsin protein is determined from the measured concentration and the volume, and compared to that of a normal healthy person. However, it does not disclose what the renal functions are nor does it disclose that an increased megsin concentration impairs renal function. For example, the specification does not show that an increased level of megsin protein impairs renal functions such as the excretion of waste material from the bloodstream or impairs the ability to maintain serum electrolyte, acid-base levels or osmolality.

The specification on page 33 discloses that since a significant difference between normal healthy persons and IgA nephrophathy patient was observed, onset of renal disorders could be confirmed by measuring megsin protein. Figure 5 of the specification indicates that megsin protein is increased in IgA patients as compared to normal patients.

The specification lacks a clear written disclosure of how the amount (concentration) of megsin protein in a biological specimen may be used to evaluate renal functions. At best, an increased amount of megsin protein in a patient as compared to a normal healthy individual can be used to determine onset of renal disorders. Such is not seen as sufficient to support the breath of the claims and without this disclosure, one skilled in the art cannot practice evaluating renal functions without undue experimentation because in order to evaluate renal functions, one skilled in the art would have to know what the renal functions are and how megsin protein specifically effects these renal functions.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3, 5, and 6-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear how determining the amount of megsin protein correlates to renal function. Does an increase or a decrease in the amount of megsin protein indicate renal function?

Claim 1, part (b) the recitation "said sample" is vague and indefinite. It is unclear if applicant is referring to the biological specimen recited in part (a) or if applicant is referring to something else. Please clarify.

Claim 1 is vague and indefinite because it is unclear what relationship exists between the anti-megsin protein antibody and the megsin protein. The claim merely recites the addition of an anti-megsin protein without indicating the purpose. Does the antibody bind the megsin protein and then the complex is detected to determine the presence of the megsin protein in the sample?

Claim 6, line 2 the recitation "against" is vague and indefinite. It is unclear what applicant intends. Does applicant intend that the antibody binds the amino acid sequence or does applicant intend the antibody comes in contact with the amino acid sequence or does applicant intend something else? Please clarify. See also deficiencies found in claim 8.

Claim 12 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble recites a method of detecting megsin protein. However, there is no positive recitation in the body of the claim of a megsin protein. Is the amino acid sequence of SEQ ID NO: 11, 12, 14 or 17 part of a megsin protein or do these SEQ ID's refer to something else?

Claim 12, part (ii) is vague and indefinite because it is unclear which antibody is bound to the antigen. The claim recites a first and second antibody, but only one antibody has formed a complex with the antigen. Further, it is unclear what the antigen

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is? Is it the megsin protein recited in the preamble the antigen or is it SEQ ID: 11, 12, 14 or 17 the antigen?

Claim 12 the recitation "against" is vague and indefinite. It is unclear what applicant intends. Does applicant intend that the antibody binds the amino acid sequence or does applicant intend the antibody comes in contact with the amino acid sequence or does applicant intend something else? Please clarify.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 6 and 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Tsumimoto et al., (Purification, cDNA Cloning and Characterization of a New Serpin with Megakaryocyte Maturation Activity, Journal of Biological chemistry, vol 272, No. 24, June 1997).

Tsujimoto et al disclose a protein comprised of amino acid sequence consisting of 380 residues. Tsujimoto et al disclose monoclonal antibodies directed to the protein which are used to detect the protein (p. 15377). Tsujimoto et al disclose the protein comprises SEQ ID 11 (p. 15377, Fig. 5 Factor, line 1 – Factor line 2,

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FREMDDNQGNVFF, same as SEQ ID 11 of applicants specification on page 28).

Tsujimoto et al disclose the protein comprises SEQ ID 12, (p. 15377, Fig. 5 Factor, line 3, SQSGLQSQLKRVFSD, same as SEQ ID 12 of applicants specification on page 28).

Tsujimoto et al disclose the protein comprises SEQ ID 14, (p. 15377, Fig. 5 Factor, line 7, NLMEWTNPRRMTSKYV, same as SEQ ID 14 of applicants specification on page 28). Therefore, Tsumimoto et al an antibody directed to amino acid sequences comprising SEQ ID's 11, 12 and 14.

With respect to the megsin protein as recited in the instant claims. Even though Tsujimoto et al does not explicitly state that the protein is megsin, it is inherent that the amino acid residue constitute the megsin protein. Therefore, since Tsujimoto et al disclose monoclonal antibodies directed to this protein, Tsujimoto et al anticipates the instantly recited claims.

7. Claim 6 is rejected under 35 U.S.C. 102(e) as being anticipated by Tsujimoto et al. (US 5,831,030).

Tsujimoto et al disclose antibodies that bind to an amino acid sequence that comprises SEQ ID's 11, 12 and 14 (columns 39-42 and claims 1 and 2). Therefore, Tsujimoto et al anticipates the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 6-9 and 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gombinski (US 6,297,062) in view of Tsujimoto et al., (Purification cDNA Cloning and Characterization of a New Serpin with Megakaryocyte Maturation Activity, Journal of Biological Chemistry, vol 272, No. 24, June 1997).

Gombinski disclose methods for detecting and determining biological entities in a test sample. Gombinski disclose magnetic particles which may have antibodies immobilized on the surface of the particles. Gombinski disclose that these magnetic particles containing the immobilized antibody will bind to the biological entity. Gombinski disclose that this biological entity can be a protein (col 3 and 4). Gombinski disclose that the magnetic particle containing the immobilized antibody and the biological entity can be further subjected to monoclonal antibodies linked to detectable markers (marker molecule) to detect the biological entity (col 12, lines 49-67). Gombinski disclose the use of a magnet with the magnetic particles. Gombinski disclose kits for carrying out the methods (col 10 and abstract). Gombinski disclose that

the sample can be any type of liquid media which may contain the biological entity to be detected.

Gombinski differ from the instant invention in failing to teach the antibodies are anti-megsin antibodies.

Tsujimoto et al disclose a protein comprised of amino acid sequence consisting of 380 residues. Tsujimoto et al disclose monoclonal antibodies designated 35 and 336 directed to the protein which are used to detect the protein (p. 15377). Tsujimoto et al disclose the protein comprises SEQ ID 11 (p. 15377, Fig. 5 Factor, line 1 – Factor line 2, FREMDDNQGNVFF, same as SEQ ID 11 of applicants specification on page 28). Tsujimoto et al disclose the protein comprises SEQ ID 12, (p. 15377, Fig. 5 Factor, line 3, SQSGLQSQLKRVFSD, same as SEQ ID 12 of applicants specification on page 28). Tsujimoto et al disclose the protein comprises SEQ ID 14, (p. 15377, Fig. 5 Factor, line 7, NLMEWTNPRRMTSKYV, same as SEQ ID 14 of applicants specification on page 28). Therefore, Tsumimoto et al an antibody directed to amino acid sequences comprising SEQ ID's 11, 12 and 14.

It would have been obvious to one of ordinary skill in the art to use the antibodies taught by Tsujimoto et al in the method and kit of Gombinski because Gombinski is generic with respect to the biological entity (analyte) that is to be detected and one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case megsin protein.

11. Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rohr (US 5,445,970) in view of Tsujimoto et al., (Purification, cDNS Cloning and

Characterization of a New Serpin with Megakaryocyte Maturation Activity, Journal of Biological Chemistry, Vol 272, No. 24, June 1997).

Rohr disclose magnetic particles (granules) having binding members immobilized on the surface (col 6, lines 36-62). Rohr disclose that these binding members can be antibodies (col 5). Rohr disclose that these magnetic particles are used to determine the presence or amount of analyte in a test fluid. Rohr disclose that this test fluid can be urine (col 4, lines 59-68). Rohr disclose that these magnetic particles can be used to determine any analyte of interest for which there exists a naturally occurring binding member or for which a binding member can be prepared.

Rohr differs from the instant invention in failing to specifically teach that the antibody is anti-megsin antibody.

Tusujimoto et al disclose a protein comprised of amino acid sequence consisting of 380 residues. Tusujimoto et al disclose monoclonal antibodies directed to the protein which are used to detect the protein (p. 15377). Tsujimoto et al disclose the protein comprises SEQ ID 11 (p. 15377, Fig. 5 Factor, line 1 – Factor line 2, FREMDDNQGNVFF, same as SEQ ID 11 of applicants specification on page 28). Tsujimoto et al disclose the protein comprises SEQ ID 12, (p. 15377, Fig. 5 Factor, line 3, SQSGLQSQLKRVFSD, same as SEQ ID 12 of applicants specification on page 28). Tsujimoto et al disclose the protein comprises SEQ ID 14, (p. 15377, Fig. 5 Factor, line 7, NLMEWTNPRRMTSKYV, same as SEQ ID 14 of applicants specification on page 28). Therefore, Tsumimoto et al an antibody directed to amino acid sequences comprising SEQ ID's 11, 12 and 14.

It would have been obvious to one of ordinary skill in the art to use the antibodies taught by Tusujimoto et al in the method of Rohr because Rohr specifically teaches that magnetic particles can be used to determine any analyte of interest for which there exists a naturally occurring binding member or for which a binding member can be prepared and thus, one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case megsin protein.

With respect to the megsin protein as recited in the instant claims. Even though Tusujimoto et al does not explicitly state that the protein is megsin, it is inherent that the amino acid residue constitute the megsin protein. Therefore, since Tusujimoto et al disclose monoclonal antibodies directed to this protein, Tusujimoto et al anticipates the instantly recited claims.

Response to Arguments

12. Applicant's arguments filed June 7, 2004 have been fully considered but they are not persuasive.

Applicant argues that Tsujimoto et al do not disclose the specific amino acid sequences of megsin protein. This is not found persuasive because Tsumimoto et al does teach the specific amino acid sequences recited in the instant claims (see above 102(a) rejection). Applicant further argues that Tsujimoto et al did not disclose or suggest antibodies against partial peptides of megsin protein. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., against partial peptides of megsin protein) are not recited in the rejected claim(s). Although the claims are

interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the combination of Gombinski and Tsujimoto et al is not obvious in the absence of applicant teachings. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Applicant further argues that the antibodies of Tsujimoto et al are raised against the entire protein as the immunogen and that applicant has utilized partial peptides of the megsin protein which show low identity with other members of the serpin family and are hydrophilic as immunogens. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., partial peptides of the megsin protein which show low identity with other members of the serpin family and are hydrophilic as immunogens) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the Rohr and Tsujimoto are not obviously combinable with each other and that they have been combined here by utilizing the hindsight provided by

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applicant's teachings. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gary W. Counts
Examiner
Art Unit 1641
September 21, 2004



LONG V. LE
SUPERVISORY PATENT EXAMINER
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09/27/04